REMARKS

At the outset, Applicant wishes to thank the Examiner for her assistance through telephonic interviews.

Status of the Claims

Claims 1-11 are currently pending. In the present Response, claims 1-9 are cancelled; claims 10-11 are amended; and new claims 12-19 are added. Thus, after entry of these amendments, claims 10-19 are presented for consideration.

Pursuant to the Office Action, claims 1-5 remain rejected under 35 U.S.C. §101 for allegedly being directed to non-statutory subject matter. Claims 1-11 remain rejected under 35 U.S.C. §112, first paragraph, for allegedly not enabling a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claims 1-11 remain rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Support for the Claim Amendments

Support for new claims drawn to an isolated mouse strain from BALB/C mice having the trait of developing rheumatoid arthritis can be found throughout the specification, in particular, support can be found, *inter alia,* in Example 1; on page 6, lines 3-10; in Examples 2 to 9; and Figures 1, 3, 5, 7, 9, 11, and 13-16. Support for new claims drawn to methods for producing a mouse strain from BALB/C mice comprising a trait of developing rheumatoid arthritis can be found, *inter alia,* in Example 1. New and amended claims which include the symptoms of rheumatoid arthritis can be found, *inter alia,* on page 3, line 25, to page 4, line 14; in Examples 1 to 9; and Figures 1, 3, 5, 7, 9, 11, and 13-15. Applicants also submit the Notice from the International Depositary Authority providing the accession number of the mouse deposited with the International

Depositary Authority according to the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure.

Applicant respectfully requests entry of the amendments set forth in this response under 37 CFR §1.116. The amendment places the case in condition for allowance and places the case in better condition for appeal; the amendment does not raise any issues of new matter; and, the amended and new claims do not present new issues requiring further consideration or search.

Rejection under 35 U.S.C. §101

Claims 1-5 remain rejected under 35 U.S.C. §101 for allegedly claiming an invention directed to non-statutory subject matter. Applicant respectfully traverses this rejection; however, in order to further prosecution of the present application, Applicant cancels claims 1-5, without prejudice.

Applicant has added new independent claim 12 and dependent claims 13 to 14. To the extent that similar rejections may be raised against the new claims, Applicant provides the following reasons for the patentability of the claims.

The Office Action states that to be patentable, claims cannot read on a product of nature. Applicant respectfully submits that Applicant's claimed isolated mouse strain is not a product of nature. In other words, the claimed mouse strain has been altered by the hand of man.

As stated in the specification, and declared in the Rule 132 Declaration (submitted 2/1/01), Applicant, in looking to develop a mouse model with natural onset of morbid conditions strikingly similar to those of rheumatoid arthritis, purchased ordinary BALB/C mice from Nippon SLC. Applicant recognized that BALB/C mice were more susceptible to autoimmune diseases upon manipulation of the immune system; however, the original strain does not spontaneously develop autoimmune disease. Therefore, random matings

of BALB/C mice in a natural environment would not spontaneously give rise to Applicant's claimed mouse strain.

Applicant interbred the purchased BALB/C mice in a closed colony for nearly a year and a half and screened the offspring before his diligence was rewarded with a female mouse with joint swelling. By interbreeding the normal BALB/C mice in a closed colony, Applicant artificially raised the incidence of mutations. Thus, Applicant respectfully submits that this artificial environment created by the Applicant was the "hand of man" that gave rise to the new phenotypically distinct strain and, further, that without such intervention, this strain would not have been produced.

On page 4 of the Office Action, it is alleged that the "female mouse (SKG mouse) was then bred to a 'normal' male mouse of the same colony; progeny of these mice displayed the joint swelling. Declarant Sakaguchi indicates that the male mouse also bore the mutation. From these statements, it is readily apparent that not only the female SKG mouse but other mice in the colony naturally contained the mutation which results in a joint swelling phenotype. Thus the claimed mouse is a product of nature." Applicant respectfully disagrees with this interpretation. Applicant avers that the female SKG mouse, as well as the male mouse that was mistakenly identified as "normal," arose in the same artificial environment. As such, they are both mice of Applicant's claimed invention.

Applicant further submits that by carefully monitoring the offspring and selectively breeding promising pairs, Applicant has been able to maintain and propagate the claimed mouse strain that would otherwise have been lost. As support, it should be noted that it is believed that the genetic abnormality causing natural onset of rheumatoid arthritis is autosomal and recessive. Without Applicant's intervention, by creating an unnatural, closed breeding colony and selecting promising breeding pairs, this recessive trait could quite easily have become lost.

The Patent Office also alleges that the specification does not provide any objective evidence that a phenotypic trait distinguishes the claimed mice from the mouse detected in Applicant's founding colony. This point is important because the disclosure of U.S. Patent No. 6,040,495 (the "'495 patent"), having issued claims directed to an inbred strain of mouse, did show that the patent mice were distinct from the original mouse strain.

In the '495 patent, a hairless ICR mouse was mated to a female hairless mouse. The offspring were mated and these brother-sister mating of the offspring were repeated for up to 70 generations to obtain the hairless mouse strain NS:Hr/ICR hairless mice. Similarly, normal BALB/C mice were mated in an artificially, closed colony for almost a year and a half to obtain Applicant's claimed mouse strain.

On page 3 of the Office Action, it is noted that Table 6 (see column 7 of the '495 patent) clearly distinguishes the NS:Hr/ICR hairless mice from the original ICR mouse in that all of the NS:HR/ICR hairless mice succumbed to a complete infection with *H. pylori* while *H. pylori* infection was slightly observed in the other test animals, including the ICR mouse. Thus, the Office Action continues, the patented mice and the original mouse strain from which the patented mice were obtained are distinct.

Analogous to situation of the '495 patent, Applicant's claimed mouse strain possesses the trait of developing natural onset of rheumatoid arthritis. This is distinct from the parent/original mouse strain (i.e., the BALB/C mice) that started Applicants closed colony, which cannot. Thus, Applicant respectfully avers that the claimed mice of the present invention are sufficiently distinct from the original mouse strain to satisfy the requirements of section 101. The specification provides objective evidence that a phenotypic trait distinguishes the claimed mouse strain from the original BALB/C mice.

The Office Action, on page 3, first full paragraph, alleges that the specification does not provide any objective evidence that a phenotypic trait distinguishes the claimed mice from the mouse detected in Applicant's colony, the mouse that naturally

(spontaneously) occurred in the colony. Applicant first wishes to point out that the mouse detected in Applicant's colony (the first female mouse with natural onset of rheumatoid arthritis) did not occur naturally. As mentioned previously, this mouse arose in an artificially maintained, closed breeding colony after nearly a year and a half of inbreeding.

Secondly, the phenotypic traits of interest to distinguish Applicant's claimed mouse strain from the original mouse strain should be between Applicant's claimed mouse stain and the original, normal BALB/C mouse strain and not between Applicant's claimed mouse strain and the first mouse with natural onset of rheumatoid arthritis bred from Applicant's closed colony.

This phenotypic difference is claimed in independent claim 12. In other words, the phenotypically distinct trait the claimed mouse has is that it develops rheumatoid arthritis. This is not a trait possessed by the normal parent BALB/C mice.

Finally, the specification provides ample objective evidence of the phenotypic differences between the claimed mouse strain and the original mouse strain (BALB/C). For example, Examples 2-5 and Figures 1-13 show the differences between the forelegs and hind legs of a normal mouse and those of the claimed mouse. Examples 6-8 and Figures 14-16 show the immunological differences between normal BALB/C mice and the claimed mice. Thus, the specification provides evidence of numerous phenotypic traits which clearly distinguish Applicant's claimed strain over the normal BALB/C parent strain.

Accordingly, in light of the amendments and the reasons provided above, Applicant respectfully submits that new claim 12 and claims 13-14, which depend from claim 12 and incorporate all the limitations thereof, are patentable and requests passage of the claims to allowance.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1-11 remain rejected under 35 U.S.C. §112, first paragraph, because the Office Action states that the specification, while being enabling for a SKG BALB/C mouse strain that develops natural onset rheumatoid arthritis, and methods of producing and using the mouse stain, does not reasonably provide enablement for an SKG BALB/C strain that develops natural onset of autoimmune arthritis, and methods for producing and using the mouse strain.

Applicant, in order to further prosecution of this application, has cancelled claims 1-9, and amended claims 10 and 11 to recite to rheumatoid arthritis. Accordingly, Applicant respectfully submits that these claim amendments overcome the rejection based upon 35 U.S.C. §112, first paragraph and requests withdrawal of the rejection as applied to claims 10-11.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1-11 remain rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action alleges that claims 1, 3, 5, 6, 8, and 10 remain vague and indefinite by the phrase "autoimmune arthritis." As Applicant has canceled claims 1-9 and amended claim 10 to replace "autoimmune arthritis" with "rheumatoid arthritis," Applicant submits that this rejection has been overcome.

The Office Action alleges that claim 10 remains confusing because it is unclear how determining whether a potential therapy decreases a symptom of autoimmune arthritis identifies a therapy that decreases a symptom of rheumatoid arthritis. Applicant has amended claim 10 to replace "autoimmune arthritis" with "rheumatoid arthritis," thus, Applicant submits that this rejection has been overcome.

The Office Action alleges that claims 1 and 6 are further rendered vague and indefinite by the phrase "derived from." As Applicant has cancelled claims 1 and 6, Applicant submits that this rejection has been overcome.

Therefore, in light of the amendments to the claims and the reasons provided, Applicant respectfully requests reconsideration and withdrawal of the rejection based upon 35 U.S.C. §112, second paragraph, as applied to remaining claims 10-11.

CONCLUSION

Claims 1-11 are pending in the application. Claims 1-9 have been cancelled; claims 10 and 11 have been amended; and new claims 12-19 have been added by the present Response. Accordingly, claims 10-19 are presented for consideration.

Applicant requests that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submits that the claims are in condition for allowance. If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant believes that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

Date: January 9, 2002

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Version with markings to show changes made

In the claims:

Claims 1-9 have been cancelled.

Claims 10 and 11 have been amended as follows:

10. (Amended) A method of identifying a therapy that decreases a symptom of rheumatoid arthritis comprising:

(a) treating a mouse of the isolated mouse strain of claim 12 with a potential therapy; and

(b) determining whether the potential therapy decreases a symptom of rheumatoid arthritis [autoimmune arthritis] in the mouse [wherein identification of a potential therapy that decreases a symptom of autoimmune arthritis in the mouse identifies a therapy that decreases a symptom of rheumatoid arthritis].

11. (Amended) The method of claim 10, wherein the symptom is selected from the group consisting of: arthritis in a foreleg or hind leg joint, joint stiffening, appearance of pannus, lymphocyte infiltration into [of] joint cartilage or bone, destruction of joint cartilage or bone, production of rheumatoid factor or autoantibody against type II collagen, and hypergammaglobulinemia.